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BY EXPRESS MAIL

Assistant Commissioner for Patents
Washington, D.C. 20231

File No.: TOBINICK 3.0-007
Inventor(s): Dr. Edward L. Tobinick
Title: TUMOR NECROSIS FACTORS ANTAGONISTS FOR THE TREATMENT OF NEUROLOGICAL DISORDERS

Assignee: None

Dear Sir:

Enclosed herewith are the following documents in the above-identified application for a Letters Patent of the United States:

1 Pages of Abstract	x Verified Statement for Small Entity Status
16 Pages of Specification	Declaration, Power of Attorney & Petition
24 Number of Claims	Two (2) return-addressed postcards
-- Sheets of Drawings	(PLEASE PROVIDE FILING DATE & SERIAL NUMBER)
-- Assignment for Recording	(attached to copy of this letter)

Check No. _____ in the amount of $416.00 __, calculated as follows:

Basic Fee (**Large Business $760.00) (*Small Business $380.00)	$380.00
Additional Fees:	
Total number of claims 24	
Total number of claims in excess of 20, 4 times (**$18)(*$9)	36.00
Number of independent claims 1	
Number of independent claims minus 3, -- times (**$78)(*$39)	--
Assignment recording fee ($40)	--
Multiple dependent claims (**$260) (*$130)	--
TOTAL filing and assignment recording fees	$416.00

CONVENTION DATE _____ for _____Appln. No._____ is claimed.

Priority Document: ____Enclosed ____Will follow

Respectfully submitted,

EZRA SUTTON, Reg No. 25,770

ES/jmt
Enclosures

Applicant or Patentee: Dr. Edward L. TOBINICK / ARTHUR J. TOBINICK
Serial or Patent No.:
Filed or Issued:
Attorney's Docket No.: TOBINICK 3.0-007
Title: TUMOR NECROSIS FACTOR ANTAGONISTS FOR THE TREATMENT OF NEUROLOGICAL DISORDERS

VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS (37 CFR 1.2(f) AND 1.27(b) - INDEPENDENT INVENTOR

As a below-named inventor, I hereby declare that I qualify as an independent inventor as defined in 37 CFR 1.9(c) for purposes of paying reduced fees under Section 41(a) and (b) of Title 35, Untied States Code, to the Patent and Trademark office with regard to the invention entitled TUMOR NECROSIS FACTOR ANTAGONISTS FOR THE TREATMENT OF NEUROLOGICAL DISORDERS described in:

[X] the specification filed herewith
[ ] Application Serial No. _____, filed _____
[ ] Patent No. _____, issued _____.

I have not assigned, granted, conveyed, or licensed and am under no obligation, under contract or law to assign, grant, convey, or license, any rights in the invention to any person who could not be classified as an independent inventor under 37 CFR 1.9(c) if that person had made the invention, or to any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e).

Each person, concern, or organization to which I have assigned, granted, conveyed, or licensed or am under an obligation under contract or law to assign, grant, convey, or license any rights in the invention is listed below:

[X] no such person, concern, or organization
[ ] persons, concerns, or organizations listed below*

*NOTE: Separate verified statements are required from each named person, concern, or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

FULL NAME _____
ADDRESS _____
[ ] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION

FULL NAME _____
ADDRESS _____
[ ] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION

FULL NAME _____
ADDRESS _____
[ ] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

Dr. Edward L. TOBINICK	ARTHUR JEROME TOBINICK	
NAME OF INVENTOR	NAME OF INVENTOR	NAME OF INVENTOR
X _____	_____	
Signature of Inventor	Signature of Inventor	Signature of Inventor
X FEB. 21, 1999	Feb 21, 1999	
Date	Date	Date

TOBINICK 3.0-007

TUMOR NECROSIS FACTOR ANTAGONISTS FOR THE TREATMENT OF NEUROLOGICAL DISORDERS

FIELD OF THE INVENTION

The present invention relates to tumor necrosis factor (TNF) antagonists or TNF blockers for the treatment of neurological disorders, trauma, injuries or compression; or autoimmune neurological disorders. More particularly, the TNF antagonists or TNF blockers are used in a new treatment of these disorders by inhibiting the action of TNF in the cells of the human body. The use of these TNF antagonists or TNF blockers results in the amelioration of these neurological conditions.

BACKGROUND OF THE INVENTION

Neurological disorders due to demyelinating disease, immune disease, inflammation, trauma, or compression, occur in different clinical forms depending upon the anatomic site and the cause and natural history of the physiological problem. Common to all of these disorders is the fact that they can cause permanent neurological damage, that damage can occur rapidly and be irreversible, and that current treatment of these conditions is unsatisfactory, often requiring surgery and/or the use of pharmacologic agents, which are often not completely successful.

These neurological conditions include acute spinal cord trauma, spinal cord compression, spinal cord hematoma, cord contusion (these cases are usually traumatic, such as motorcycle accidents or sports injuries); nerve compression, the most common condition being a herniated disc causing sciatic nerve compression,

neuropathy, and pain; but also including cervical disc herniation, causing nerve compression in the neck; carpal tunnel syndrome and acute or chronic spinal cord compression from cancer (this is usually due to metastases to the spine, such as from prostate, breast or lung cancer); autoimmune disease of the nervous system, and demyelinating diseases, the most common condition being multiple sclerosis.

Steroid drugs such as cortisone that are used to treat the aforementioned neurological problems and conditions are particularly hazardous because they are used either at high dosage, with a corresponding increasing risk of side effects, or because they are used chronically, also increasing their adverse effects. Lastly, steroids are only partially effective or completely ineffective.

There remains a need for a new pharmacologic treatment of these aforementioned physiological problems of the nervous system associated with autoimmune disease, demyelinating diseases, trauma, injuries and compression with the pharmacological use of TNF antagonists or TNF blockers, which are greatly beneficial for the large number of patients whom these conditions affect. Two new drugs which are powerful TNF blockers are etanercept and infliximab. Etanercept or infliximab may be used for the immediate, short term and long term (acute and chronic) blockade of TNF in order to minimize neurologic damage mediated by TNF dependent processes occurring in the aforementioned neurological disorders. The use of these TNF antagonists or TNF blockers would

result in the amelioration of these physiological neurological problems.

DESCRIPTION OF THE PRIOR ART

Pharmacologic chemical substances, compounds and agents which are used for the treatment of neurological disorders, trauma, injuries and compression having various organic structures and metabolic functions have been disclosed in the prior art. For example, U.S. Patent Nos. 5,756,482 and 5,574,022 to ROBERTS et al disclose methods of attenuating physical damage to the nervous system and to the spinal cord after injury using steroid hormones or steroid precursors such as pregnenolone, and pregnenolone sulfate in conjunction with a non-steroidal anti-inflammatory substance such as indomethacin. These prior art patents do not teach the use of a TNF antagonist or TNF blocker for the suppression and inhibition of the action of TNF in the human body to treat neurological trauma, injury or compression, or autoimmune neurologic disease as in the present invention.

U.S. Patent No. 5,605,690 to JACOBS discloses a method for treating TNF-dependent inflammatory diseases such as arthritis by administering a TNF antagonist, such as soluble human TNFR (a sequence of amino acids), to a human. This prior art patent does not teach the use of a TNF antagonist or TNF blocker for the suppression and inhibition of the action of TNF in the human body to treat neurological trauma, injury or compression, or autoimmune neurologic disease, as in the present invention.

U.S. Patent No. 5,656,272 to LE et al discloses methods of treating TNF-alpha-mediated Crohn's disease using chimeric anti-TNF antibodies. This prior art patent does not teach the use of a TNF antagonist or TNF blocker for the suppression and inhibition of the action of TNF in the human body to treat neurological trauma, injury or compression, or autoimmune neurologic disease, as in the present invention.

U.S. Patent No. 5,650,396 discloses a method of treating multiple sclerosis (MS) by blocking and inhibiting the action of TNF in a patient. This prior art patent does not teach the use of the TNF antagonist as in the present invention.

None of the prior art patents disclose or teach the use of the TNF antagonist or TNF blocker of the present invention for suppression and inhibition of the action of TNF in a human to treat neurological injury, trauma or compression, or autoimmune neurologic disease, in which the TNF antagonist gives the patient a better opportunity to heal.

Accordingly, it is an object of the present invention to provide a TNF antagonist for a new pharmacologic treatment of neurological disorders, trauma, injuries and compression affecting the nervous system of the human body, or autoimmune neurologic disease, such that the use of these TNF antagonists will result in the amelioration of these neurological conditions.

Another object of the present invention is to provide a TNF antagonist for providing suppression and inhibition of the action

of TNF in a human to treat neurological injury, trauma or compression, or autoimmune neurologic disease.

Another object of the present invention is to provide a TNF antagonist that reduces inflammation to the patient by inhibiting the action of TNF in the human body for the immediate, short term (acute conditions) and long term (chronic conditions), such that this reduction in inflammation will produce clinical improvement in the patient and will give the patient a better opportunity to heal.

Another object of the present invention is to provide a TNF antagonist that can offer acute and chronic treatment regimens for neurological conditions caused by neurological trauma, compression, injury and/or disease, such conditions including acute spinal cord injury, herniated nucleus pulposus (herniated disc), spinal cord compression due to metastatic cancer, carpal tunnel syndrome, pituitary adenoma, primary or metastatic brain tumors, chronic pain syndromes due to metastatic tumor, increased intracranial pressure, autoimmune demyelinating diseases such as multiple sclerosis, inflammatory CNS diseases, such as subacute sclerosing panencephalitis, and other related neurological disorders and diseases.

SUMMARY OF THE INVENTION

The present invention provides a method for inhibiting the action of TNF for treating neurological conditions in a human by administering to the human a dosage level of a TNF antagonist selected from the group consisting of etanercept and infliximab for reducing the inflammation of neuronal tissue of the human and/or

preventing immune system damage to neuronal tissue. The TNF antagonist is administered subcutaneously, intravenously, intrathecally, or intramuscularly.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

TNF antagonist regimens to be used for neurological disorders are designed in two general ways: acute regimens, designed to achieve rapid blood levels and rapid action, wherein TNF blockade is desired for hours to days; and chronic regimens, where TNF blockade is desired for days, weeks, or months. Currently available TNF antagonists which are suitable for these regimens are etanercept (ENBREL™) from Immunex Corporation and infliximab (REMICADE™) from Centocor, Inc. Trauma, injury, compression and other neurological disorders can affect individual nerves, nerve roots, the spinal cord, or the brain. The conditions which are of most concern here are the following:

1) acute spinal cord injury,

2) demyelinating diseases, such as multiple sclerosis,

3) herniated nucleus pulposus (herniated disc),

4) spinal cord compression due to metastatic cancer,

5) carpal tunnel syndrome (non-RA),

6) pituitary adenoma,

7) primary or metastatic brain tumors,

8) chronic pain syndromes due to metastatic tumor,

9) increased intracranial pressure, and

10) inflammatory CNS diseases, such as subacute sclerosing panencephalitis.

TNF antagonists are a novel way to treat neurologic trauma, injury, compression and neurological disorders in comparison with steroids. Experimental evidence has shown that excessive levels of TNF are released by injury to neuronal tissue. Accordingly, the use of TNF antagonists will result in amelioration of these neurological conditions. Because of the profoundly powerful action of the new TNF antagonists that have recently become available these agents can prevent neurologic injury in a unique way, filling an urgent clinical need for more effective therapy. Also, because of the extremely safe side effect profile of these agents, they can be used either singly or in combination with other pharmacologic agents. Specifically, TNF antagonists can safely be used with steroids, which are the only other class of agents which have been shown to be beneficial for certain of these conditions. Importantly, the TNF antagonists lack the adverse effects of steroids as previously described. Lastly, steroids are only partially effective or completely ineffective.

More detailed discussion of each of these clinical conditions is as follows:

1) Acute spinal cord injury:

About 10,000 cases occur per year in the U.S., with a current population of over 200,000 patients with residual neurologic damage, many of whom are paralyzed (quadriplegia or paraplegia). Current treatment for the acute injury is inadequate. In the early

1990's it was shown that early (within 8 hours of injury) treatment with high doses of steroids (methyl prednisolone) was beneficial for some of these patients. Surgical stabilization and spinal decompression is often necessary because of excessive swelling (edema) which can itself cause further severe injury to the cord due to further compression of the cord against its bony spinal canal. The etiology of most of these cases are motor vehicle accidents, with the remainder being sports injuries, falls, and other accidents. The window of opportunity for treatment is small, since massive swelling can occur within minutes.

The treatment regimen used here would be the acute regimen. This could involve any of the TNF antagonists, but currently etanercept would be the leading candidate. Etanercept is currently approved only for rheumatoid arthritis, and is used as a subcutaneous injection of 25mg used twice a week. This regimen produces peak blood levels in an average of 72 hours. A preferred method for acute spinal cord injury involves intravenous infusion to produce more rapid serum levels and higher levels than achieved by SC injection. This is a new method of dosing that is not being used for arthritis. This acute regimen is a unique delivery method for etanercept and is uniquely necessary for clinical neurologic conditions requiring rapid blockade of TNF.

2) Herniated nucleus pulposus (herniated disc):

Low back pain affects 70% of the population during their lifetime, with 25% of this group having pain in the sciatic distribution. Current pharmacologic treatment is inadequate,

consisting of analgesics and anti-inflammatory medications (such as nonsteroidal anti-inflammatories (NSAIDS), such as ibuprofen (Motrin, etc.) and epidural steroid injections (generally regarded as having limited usefulness). Many of these patients eventually have surgery. Complications of lumbar disc herniation include permanent damage to the sciatic nerve, causing muscle weakness and atrophy in the lower extremity. Acute herniation with rapid onset of pain and sciatic nerve symptoms could be treated with the above acute regimen with or without addition of the chronic regimen (described below) if symptoms continued. Treatment could also be reserved for patients not responding to conventional therapy. The acute treatment regimen, as outlined above, could be used for patients in whom rapid control of symptoms was desired. Most patients, however, would be treated conservatively and conventionally at first, with TNF blockade using one of the chronic regimens below added later for nonresponders. Herniated cervical discs would be treated the same way as herniated lumbar discs with the need for careful evaluation by a neurologist, neurosurgeon, and/or orthopedic surgeon for signs of neurologic compromise kept in mind. The chronic treatment regimen includes subcutaneous etanercept of 25mg (dosage range 10mg to 50mg) once or twice a week; or infliximab administered by intravenous infusion once every two months (range once per month to once per six months).

3) Spinal cord compression due to metastatic cancer:

Cord compression due to metastatic cancer is a catastrophic event leading to rapid paralysis if not quickly diagnosed and

treated. It is most common with cancers of the breast, colon, lung and prostate, but can be a complication of metastatic disease from a wide variety of malignancies, including melanoma and multiple myeloma. Current treatment regimens include high dose steroids, emergency radiation treatment, and/or emergent surgical decompression. Paralysis can occur within hours, so treatment must be initiated within this time period to avoid permanent sequelae. The mechanism of action of TNF blockage here would be similar to that above. In addition, it is possible that TNF blockade could be directly tumoricidal or tumoristatic with certain malignancies. Impending cord compression could be treated with the chronic regimen. However, as explained above, most patients would need to be emergently treated with the acute regimen, as outlined above.

4) Carpal Tunnel Syndrome (CTS) (non-RA):

Carpal tunnel syndrome involves compression of the median nerve at the wrist, causing pain and neurologic symptoms in the hand. It is a common condition, being aggravated by repetitive stress injury (RSI) in the workplace (such as typists and writers, manual laborers, etc.), and is also a complication of rheumatoid arthritis (RA). Use of TNF blockade for carpal tunnel syndrome in patients with established RA would likely be covered by the existing arthritis medication for treating RA. But most patients with carpal tunnel syndrome do not have RA; they either have idiopathic CTS or CTS caused by RSI. CTS is a major cause of disability and responds poorly to current treatment regimens, which include NSAIDS, wrist splinting, and injection of steroids. The

chronic treatment regimen as outlined above would be used for the treatment of CTS (non-RA type).

5) Pituitary Adenoma:

Benign pituitary tumors grow adjacent to the optic chiasm. Unrestrained growth causes compression of the optic nerve, causing visual field defects and eventuating in blindness. Treatments include radiation, surgical decompression and bromocriptine. TNF blockade could prove to be a valuable adjunctive therapy, and could be either acute or chronic, depending on the clinical picture.

6) Primary or Metastatic Brain Tumors:

Primary brain tumors can be either benign (most commonly meningioma) or malignant (usually gliomas). Metastatic brain tumors can be from any source, most commonly lung cancer, breast cancer, or other malignancies such as melanoma. Treatment for these tumors is primarily surgery or radiation, with generally poor response to chemotherapy. Many of these tumors cause surrounding edema which can cause further neurologic deterioration. TNF blockade, either acute or chronic, could be beneficial while these patients are awaiting surgery. Additionally, TNF blockade, as discussed above, could have direct tumor inhibiting properties.

7) Chronic pain syndromes due to metastatic tumor:

Pain due to metastatic cancer is inadequately treated by currently used agents. It is probable that the mechanism of action of this pain is mediated in part by the overproduction of TNF. TNF blockade could be beneficial for selected tumors, particularly bone metastases where compression is involved. The chronic treatment

regimens would be used. One general note of caution when treating malignancies is necessary: While TNF blockade is likely to have an antitumor effect with certain malignancies, it is also possible that TNF blockade could increase growth rates with certain malignancies.

8) Elevated Intracranial Pressure (EICP):

EICP can be idiopathic (Pseudotumor cerebri) or caused by certain drugs (vitamin A excess, isotretinoin, tetracyclines, etc.) caused by malignancy (as above), or by benign tumors (e.g. cystercircosis). TNF blockade, either acute or chronic, could be helpful.

OPERATION OF THE PRESENT INVENTION

1) Chronic regimen dosing with etanercept

For adults the dose is 25mg subcutaneously (range 10mg to 50mg) administered in a range of twice a week to once a month. The initial regimen being 25mg subcutaneously twice a week and for children 0.4mg/kg given twice a week. Expected serum concentrations with this regimen would be about 3.0mcg/mL, with a desired range between 0.5 and 10mcg/mL. Other routes for chronic administration could include IM or IV dosing regimens.

2) Acute regimen dosing with etanercept

Acute treatment regimens include administration of etanercept by SC, IM, IV and intrathecal dosing routes for acute administration.

2A) Acute IV regimen with etanercept

Etanercept is administered by IV infusion in a quantity sufficient to produce a serum concentration in the range of 0.5mg/mL to 50mg/mL.

2B) Acute IM regimen for etanercept

Etanercept is given by intramuscular administration in a dose of 50mg having a range of 25mg to 100mg.

2C) Acute Intrathecal regimen with etanercept

There may be clinical use for etanercept in the cerebrospinal fluid, such as for treatment of CNS lesions (brain tumors, cord compression). Intrathecal therapy means introducing the TNF antagonist into the cerebrospinal fluid of the patient. The exact dosage is on the order of 10mg (range 1mg to 50mg).

3) Chronic treatment regimen with infliximab

Chronic indications for infliximab include herniated nucleus pulposus (herniated disk), carpal tunnel syndrome, pituitary adenoma, demyelinating disease, primary or metastatic brain tumors and chronic pain syndromes due to metastatic tumor.

Usual dosage for infliximab is 5mg/kg given by IV infusion every two months with a range of 2.5mg/kg to 20mg/kg given every 2 weeks to 2 months.

4) Acute treatment regimen with infliximab

Acute indications for infliximab include acute spinal cord injury, acute demyelinating disease, spinal cord compression and increased intracranial pressure.

The dosage for infliximab used for the acute regimen is 10mg/kg administered by IV infusion once (range 2.5mg/kg to 25mg/kg). For acute spinal cord injury only the intrathecal administration of infliximab is 0.3mg/kg having a range of 0.1mg/kg to 1mg/kg.

5) Treatment with existing regimens

The treatment regimens of the present invention may be used in conjunction with or in place of existing treatments, such as steroids and surgery. When the treatment regimens of the present invention are used concurrently with currently available treatments, the results are additive and therefore beneficial.

ADVANTAGES OF THE PRESENT INVENTION

Accordingly, an advantage of the present invention is that it provides a TNF antagonist for a new pharmacologic treatment of neurological disorders, trauma, injuries and compression affecting the nervous system of the human body, or autoimmune neurologic disease, such that the use of these TNF antagonists will result in the amelioration of these neurological conditions.

Another advantage of the present invention is that it provides for a TNF antagonist for providing suppression and inhibition of the action of TNF in a human to treat neurological injury, trauma or compression, or autoimmune neurologic disease, or inflammatory disease of the nervous system.

Another advantage of the present invention is that it provides a TNF antagonist that reduces and prevents further neurological inflammation to the patient by inhibiting the action of TNF in the

human body for the immediate, short term (acute conditions) and long term (chronic conditions), such that this reduction and prevention of inflammation will produce clinical improvement in the patient and will give the patient a better opportunity to heal.

Another advantage of the present invention is that it provides for a TNF antagonist that can offer acute and chronic treatment regimens for neurological conditions caused by neurological trauma, compression, injury and/or disease, such conditions including acute spinal cord injury, herniated nucleus pulposus (herniated disc), spinal cord compression due to metastatic cancer, carpal tunnel syndrome (non-RA), demyelinating disease, pituitary adenoma, primary or metastatic brain tumors, chronic pain syndromes due to metastatic tumor, increased intracranial pressure, and other related neurological disorders and diseases.

Another advantage of the present invention is to provide a TNF antagonist to treat neurologic disorders in humans either acutely or chronically by blocking the action of TNF and thereby modulating the immune response affecting neuronal tissue.

A latitude of modification, change, and substitution is intended in the foregoing disclosure, and in some instances, some features of the invention will be employed without a corresponding use of other features. Accordingly, it is appropriate that the appended claims be construed broadly and in a manner consistent with the spirit and scope of the invention herein.

WHAT IS CLAIMED IS:

1. A method for inhibiting the action of TNF for treating neurological conditions in a human by administering a TNF antagonist for reducing the inflammation of neuronal tissue of said human, or for modulating the immune response affecting neuronal tissue of said human, comprising the step of:

a) administering a therapeutically effective dosage level to said human of said TNF antagonist selected from the group consisting of etanercept and infliximab for reducing the inflammation of neuronal tissue of said human, or for modulating the immune response affecting neuronal tissue of said human.

2. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said TNF antagonist is performed subcutaneously, intravenously, intrathecally, or intramuscularly.

3. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said dosage level is for treating neurological diseases and disorders.

4. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said dosage level is for treating neurological traumas and injuries.

5. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said dosage level is for treating acute spinal cord injury.

6. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said dosage level is for treating herniated discs.

7. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said dosage level is for treating spinal cord compression.

8. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said dosage level is for treating carpal tunnel syndrome (non-RA type).

9. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said dosage level is for treating pituitary adenoma.

10. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said dosage level is for treating primary or metastatic brain tumors.

11. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said dosage level is for treating chronic pain syndrome due to metastatic tumor.

12. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said dosage level is for treating increased intracranial pressure.

13. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said dosage level is for treating central nervous system lesions.

14. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said dosage level is for treating autoimmune neurological diseases.

15. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said dosage level is for treating multiple sclerosis.

16. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said dosage level is for treating inflammatory CNS diseases such as subacute sclerosing panencephalitis.

17. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said etanercept is performed subcutaneously in said human wherein said dosage level is in the range of 10mg to 50mg for acute or chronic regimens.

18. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said etanercept is performed subcutaneously in said human wherein said dosage level is 25mg for acute or chronic regimens.

19. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said etanercept is performed intramuscularly in said human wherein said dosage level is in the range of 25mg to 100mg.

20. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said etanercept is performed intravenously in said human wherein said dosage level produces a serum concentration in the range of 0.5 mg/ML to 50mg/mL.

21. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said etanercept is performed intravenously by infusion in said human wherein said dosage level produces a serum concentration of 10mg/mL.

22. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said infliximab is performed subcutaneously in said human wherein said dosage level is in the range of 0.1mg/kg to 2.5mg/kg.

23. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said infliximab is performed intramuscularly in said human wherein said dosage level is in the range of 0.1mg/1kg to 2.5mg/kg for acute or chronic regimens.

24. A method for inhibiting the action of TNF in accordance with Claim 1, wherein the step of administering said infliximab is performed intravenously in said human wherein said dosage level produces a serum concentration in the range of 2.5mg/kg to 20 mg/kg.

ABSTRACT OF THE DISCLOSURE

A method for inhibiting the action of TNF for treating neurological conditions in a human by administering a TNF antagonist for reducing damage to neuronal tissue or for modulating the immune response affecting neuronal tissue of the human. The TNF antagonist administered is selected from the group consisting of etanercept and infliximab. The TNF antagonist is administered subcutaneously, intravenously, intrathecally, or intramuscularly.

DECLARATION FOR PATENT APPLICATION

Docket No. TOBINICK 3.0-007

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled TUMOR NECROSIS FACTOR ANTAGONISTS FOR THE TREATMENT OF NEUROLOGICAL DISORDERS, the specification of which

(check one) ☒ is attached hereto.

☐ was filed on _____ as Application Serial No. _____ and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)			Priority Claimed	
(Number)	(Country)	(Day/Month/Year Filed)	Yes	No
(Number)	(Country)	(Day/Month/Year Filed)	Yes	No
(Number)	(Country)	(Day/Month/Year Filed)	Yes	No

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

(Application Serial No.)	(Filing Date)	(Status—patented, pending, abandoned)
(Application Serial No.)	(Filing Date)	(Status—patented, pending, abandoned)

I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

Ezra Sutton, Reg. No. 25,770

Address all telephone calls to _____ at telephone no. (732) 634-3520.

Address all correspondence to EZRA SUTTON, P.A.
Plaza 9, 900 Route 9
Woodbridge, New Jersey 07095.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole or first inventor Dr. Edward L. TOBINICK

Inventor's signature X _____ Date X FEBRUARY 21, 1999

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(Supply similar information and signature for third and subsequent joint inventors)